Remarks

Claims 14 and 33-51 are pending in the application. In response to the Official Action mailed March 10, 2005, Claims 12 and 15 have been cancelled. In accordance with the Examiner's helpful suggestion, the subject matter of Claims 12 and 15 have been incorporated into new Claims 42 and 41, respectively. Claims 14 and 33-40 have been amended to clarify that the claims are directed to a pharmaceutical composition. Support for the amendments are found, for example, in paragraph 0013, part "Summary of the Invention" of the specification. New Claims 43-51 have been added to affirmatively recite that the pharmaceutical composition includes a therapeutically effective amount of the pulsed antigen presenting cell and a pharmaceutically acceptable carrier.

In view of the above amendments and the following remarks, the Applicants respectfully request reconsideration and withdrawal of the rejections and objections set forth in the Official Action.

Rejection Under U.S.C. §102

Claims 14-15 and 33-35 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Lisziewicz et al. (U.S. PreGrant Pub. No. 20030095988). Amended Claim 14 is directed to "A pharmaceutical composition, comprising an antigen presenting cell pulsed with an inactivated non-recombinant human immunodeficiency virus (HIV), wherein the composition expands expression of virus-specific CD8+ cells". As such, the pharmaceutical composition of the present invention is useful for the in vivo treatment by its administration to a mammal in need thereof.

The preamble "A pharmaceutical composition" of each of Claims 14 and 33-42 clearly describes the essence of the invention. In such a case, the preamble must be construed as defining the invention for purposes of comparing it to the prior art. As explained in MPEP § 2111.02, if the preamble is necessary to give life, meaning and vitality to the claim, then the claim preamble should be construed as if it appears in the balance of the claim. An example provided in the MPEP is that of *Kropa v. Robie*, 88 USPQ 478, 481 (CCPA 1951), in which the court held that the preamble "An abrasive material" further defined the structure of the claimed article. In *Kropa*, no affirmative recitation in the body of the claim indicated that the article was abrasive. Thus, the preamble breathed life and meaning into the claim and was deemed to

further define the invention. Much like *Kropa*, the bodies of Claims 14 and 33-42 do not recite that the claimed composition is a pharmaceutical. Therefore, the preamble is essential to point out the invention defined by the claims. Because the preamble "A pharmaceutical composition" breaths life, meaning and vitality into the claims, the preamble must be given patentable weight.

Lisziewicz *et al.* discloses the use of a hydroxyurea-containing HAART (Highly Active Antiretroviral Therapy) regimen for increasing the competence of a patient's immune system through structured treatment interruptions (STI), a so called autologous vaccination technique. *See* paragraphs [0009] and [0007]. Thus, Lisziewicz teaches to one of skill in the art a pharmaceutical composition that includes hydroxyurea-containing HAART, and a method of autovaccination corresponding to the treatment of infected patients with interrupted periods of administration (STI) of said pharmaceutical composition. The goal of Lisziewicz is to maintain a viral load between a low antigen threshold and a high antigen threshold in order to induce a vigorous immune response without exhausting the immune system. *See*, Fig. 1, Para. 0027. The Lisziewicz method allegedly enables the infected patient's immune system to control the pathogen after treatment has stopped. *See,* Examples 1-3, and Claims 1-69. The pharmaceutical composition provided to patients includes hydroxyurea-containing HAART, but does not include dendritic cells pulsed with inactivated HIV.

The Applicants acknowledge, however, that Lisziewicz discloses an *in vitro* analysis of the activation of STI treated patients' HIV-specific T-cells by a CTL assay. The *in vitro* assay involves a composition comprising dendritic cells obtained from the patients and pulsed with a purified heat-inactivated HIV antigen. *See,* paragraphs 0144 to 0153. Thus, Lisziewicz teaches to one of skill in the art a diagnostic test for immune system competence against HIV, which involves the steps of testing the viral load in the plasma and the *in vitro* specific interferon-gamma production in different cell types. *See* Example 4, and Claims 70-82.

Lisziewicz does not describe the use of the assay composition for injection into a patient or for any other purpose that would be considered pharmaceutical. Further, Lisziewicz provides no suggestion that antigen-presenting cells pulsed with an inactivated non-recombinant HIV would be useful for the treatment of HIV infected patients by its administration. Thus, Lisziewicz fails to suggest the use of these cells as a pharmaceutical composition. Because Lisziewicz does not describe or suggest an essential element of the claims, it does not anticipate, or render obvious, Claims 14 and 33-42.

In light of the foregoing, the Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §102(a) rejection.

Rejection Under U.S.C. §103(a)

Claims 36-38 have been rejected under U.S.C. §103(a) as allegedly being anticipated by Lisziewicz in view of Grovit-Ferbas. As explained above, Lisziewicz discloses an *in vitro* diagnostic test, in which antigen-presenting cells have been pulsed with a purified heat-inactivated HIV antigen in order to analyze T-cell specific response.

Grovit-Ferbas, like Lisziewicz, only discloses an *in vitro* diagnostic test corresponding to an ELISPOT assay for IFN-γ production, in which antigen-presenting cells from HIV infected patients have been pulsed with a heat- or chemically-inactivated recombinant HIV virus. The actual vaccine proposed by Grovit-Ferbas includes inactivated HIV, but does not include antigen-presenting cells pulsed with an inactivated recombinant HIV. The purpose of the Grovit-Ferbas assay is to analyze the ability of the inactive vaccine preparation (*i.e.*, the heat- or chemically-inactivated recombinant HIV) to elicit an Ag-specific recall response. Specifically, the assay measures, *in vitro*, whether heat-inactivated HIV-1 can stimulate AG-specific memory cells to produce IFN-γ. *See*, page 5806, first column, first full paragraph.

Consequently, Grovit-Ferbas only teaches to one of skill in the art a pharmaceutical composition consisting of heat- and chemically inactivated recombinant HIV virus, which could allegedly be useful as a HIV vaccine composition. *See*, page 5802, second column, last paragraph to page 5803, first column, first paragraph.

Thus, there is no suggestion or motivation in the teachings of Grovit-Ferbas and Lisziewicz that a composition comprising an antigen-presenting cell pulsed with an inactivated human immunodeficiency virus (HIV) can be used for the treatment of HIV infected patients by its administration. As such, the combination of Grovit-Ferbas and Lisziewicz provides no suggestion to use antigen-presenting cells pulsed with inactivated HIV. In conclusion, Lisziewicz in view of Grovit-Ferbas does not disclose nor suggest to one of skill in the art the pharmaceutical composition according to the invention.

Claims 12 and 39-40 have been rejected under U.S.C. §103(a) as allegedly being unpatentable over Lisziewicz in view of Cohen (applied to Claim 12); and in view of Grovit-Ferbas in further view of Cohen (as applied to Claims 39-40).

Considering these prior art documents, and to establish a *prima facie* case of obviousness, three basic criteria must be met:

1) there must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or to combine reference teachings;

2) there must be a reasonable expectation of success; and

3) finally, the prior art reference (or references when combined) must teach or suggest all the claimed limitations. MPEP § 2143.

The mere fact the references can be combined or modified does not render resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

As explained above, Grovit-Ferbas and Lisziewicz merely teach to one of skill in the art a pharmaceutical composition consisting of heat- and chemically-inactivated recombinant HIV virus, and a pharmaceutical composition having hydroxyurea-containing HAART, respectively.

Cohen teaches to one of skill in the art a method for inducing dendritic cells from monocytes, which have been isolated from a patient. The obtained dendritic cells are pulsed with a patient's tumor cell lysate (*i.e.*, an autologous antigen) or with antigen derived peptide (*i.e.*, a non-autologous antigen). With respect to HIV, Cohen merely indicates that dendritic cells can be challenged with antigens from the surface of HIV-1. *See,* Examples. According to Cohen, the composition comprising the pulsed dendritic cells can be used for the *in vivo* treatment of patients.

Nevertheless, Cohen does not describe dendrtitic cells pulsed with an inactivated non-recombinant HIV virus. Further, Cohen fails to discuss any *in vivo* treatment efficacy from the administration of dendritic cells challenged with antigens from the surface of HIV-1, let alone from dendritic cells pulsed with an inactivated non-recombinant HIV virus. None of the data presented therein is predictive of how dendritic cells would specifically interact with non-recombinant inactivated HIV virus, or of how dendritic cells pulsed with the virus would be able to elicit a protective immune response after administration to a patient. Thus, Cohen utterly fails to make any showing of efficacy in treating an HIV patient using even the dendritic cells challenged with antigens mentioned therein, and certainly not using dendritic cells pulsed with an inactivated non-recombinant HIV virus. Therefore, a fair reading of Cohen would provide

one skilled in the art with no reasonable expectation of successfully using dendritic cells pulsed with an inactivated non-recombinant HIV virus to treat a patient infected with HIV.

Cohen clearly does not describe the pharmaceutical composition of this invention. There being no reasonable expectation of success, Cohen also provides no suggestion to create such a pharmaceutical composition. Moreover, the brief passage in Cohen that mentions antigens from the surface of HIV-1 provides no details regarding how a pharmaceutical composition having dendritic cells challenged with antigens from the surface of HIV-1 could be made or used, much less a composition having dendritic cells pulsed with an inactivated non-recombinant HIV virus. As such, the disclosure of Cohen is also non-enabling. For these reasons, Cohen provides neither a suggestion to provide a pharmaceutical composition having dendritic cells pulsed with inactivated virus in general, nor any composition comprising dendritic cells specifically pulsed with inactivated human immunodeficiency virus.

In view of the teaching of Grovit-Ferbas and Lisziewicz, there is no suggestion or motivation for one of skill in the art to combine the compositions disclosed in *in vitro* diagnostic tests with the general pharmaceutical composition described in Cohen. In light of the foregoing, the Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection.

New Claims

New Claims 43-51 have been added to the application to further distinguish the invention over the *in vitro* assays of Grovit-Ferbas and Lisziewicz. For the reasons set forth above, the preambles of Claims 14 and 33-42 clearly distinguish those claims from the references of record. New claims 43-51 are patentable for the same reasons. In addition, the new claims affirmatively recite that the composition includes a therapeutically effective amount of the pulsed antigen presenting cell and a pharmaceutically acceptable carrier. Neither Grovit-Ferbas nor Lisziewicz describe a composition, for *in vitro* testing or otherwise, having the newly claimed features. As explained above, Cohen does not provide any suggestion to use dendritic cells pulsed with an inactivated non-recombinant HIV virus in a pharmaceutical composition. Moreover, even if Cohen did provide such a suggestion, Cohen still wholly fails to provide any indication as to what a therapeutically effective amount of those cells would be. As such, Cohen would still be non-enabled with respect to the subject matter of the new claims.

The Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested. If the Examiner believes that further minor amendments or corrections as to matters of form will advance the case, the Examiner is invited to telephone the Applicants' undersigned representative.

Respectfully submitted,

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